REMARKS / ARGUMENTS

In response to the pending Office Action of April 26, 2010, Applicants provide the following arguments and amendments. The present amendments are requested solely for the purpose of more clearly describing and claiming the present invention. The present amendments do not introduce any new matter and Applicants reserve the right to pursue the subject matter of the claims as originally presented. In light of the arguments presented and amendments requested, this application is in condition for allowance. Accordingly, entry of these amendments, reconsideration of all pending rejections and objections, and passage to allowance is respectfully requested. With the entry of this amendment, claims 1-26 are pending herein.

1. Amendments to the claims

Amendment of claim 1 is requested to add "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." Support for the requested amendment can be found throughout the specification as filed. Support for the requested amendment can be found, for example, in paragraph [0035] of the application as filed: "Generally the masking molecule will have relatively low molecular weight, for instance below 500, in particular below 200 or 150." Support for the requested amendment can also be found in paragraph [0045] of the application as filed: "Preferably however the coating molecule is a macromolecule. Thus it preferably has molecular weights at least 800, preferably at least 1000, more preferably at least 1500, most preferably at least 3000". The requested amendment to claim 1 is provided to enhance clarity and particularly point out and distinctly claim certain aspects of the present invention. The requested amendment of claim 1 does not introduce any new matter.

New claim 15 has been added which recites "The method of claim 1, wherein the masking molecule has a molecular weight less than or equal to 200 Da." Support for new claim 15 can be found throughout the specification as filed. Support for new claim

15 can be found, for example, in paragraph [0035] of the application as filed: "Generally the masking molecule will have relatively low molecular weight, for instance below 500, in particular below 200 or 150." New claim 15 does not introduce any new matter.

New claim 16 has been added which recites "The method of claim 1, wherein the masking molecule has a molecular weight less than or equal to 150 Da." Support for new claim 16 can be found throughout the specification as filed. Support for new claim 16 can be found, for example, in paragraph [0035] of the application as filed: "Generally the masking molecule will have relatively low molecular weight, for instance below 500, in particular below 200 or 150." New claim 16 does not introduce any new matter.

New claim 17 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 1000 Da." Support for new claim 17 can be found throughout the specification as filed. Support for new claim 17 can be found, for example, in paragraph [0045] of the application as filed: "Preferably however the coating molecule is a macromolecule. Thus it preferably has molecular weights at least 800, preferably at least 1000, more preferably at least 1500, most preferably at least 3000". New claim 17 does not introduce any new matter.

New claim 18 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 1500 Da." Support for new claim 18 can be found throughout the specification as filed. Support for new claim 18 can be found, for example, in paragraph [0045] of the application as filed: "Preferably however the coating molecule is a macromolecule. Thus it preferably has molecular weights at least 800, preferably at least 1000, more preferably at least 1500, most preferably at least 3000". New claim 18 does not introduce any new matter.

New claim 19 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule each have a molecular weight

greater than or equal to 3000 Da." Support for new claim 19 can be found throughout the specification as filed. Support for new claim 19 can be found, for example, in paragraph [0045] of the application as filed: "Preferably however the coating molecule is a macromolecule. Thus it preferably has molecular weights at least 800, preferably at least 1000, more preferably at least 1500, most preferably at least 3000". New claim 19 does not introduce any new matter.

New claim 20 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule are each oligonucleotides having from 5 to 150 bases." Support for new claim 20 can be found throughout the specification as filed. Support for new claim 20 can be found, for example, in paragraph [0046] of the application as filed: "Preferred types of macromolecule are oligonucleotides (e.g. 5 to 150 bases)." New claim 20 does not introduce any new matter.

New claim 21 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule are each proteins." Support for new claim 21 can be found throughout the specification as filed. Support for new claim 21 can be found, for example, in paragraph [0047] of the application as filed: "Alternative macromolecules are polypeptides, including proteins such as enzymes." New claim 21 does not introduce any new matter.

New claim 22 has been added which recites "The method of claim 1, wherein the first coating molecule and the second coating molecule are each enzymes." Support for new claim 22 can be found throughout the specification as filed. Support for new claim 22 can be found, for example, in paragraph [0047] of the application as filed: "Alternative macromolecules are polypeptides, including proteins such as enzymes." New claim 22 does not introduce any new matter.

New claim 23 has been added which recites "The method of claim 1, wherein the masking molecule is 6-mercapto-1-hexanol." Support for new claim 23 can be found

throughout the specification as filed. Support for new claim 23 can be found, for example, in the description found in paragraphs [0061] to [0063] of the application as filed. New claim 23 does not introduce any new matter.

New claim 24 has been added which recites "The method of claim 1, wherein the first coating molecule is an oligonucleotide of sequence CAGGATGGCGAACAACAAGA–thiol and the masking molecule is 6-mercapto-1-hexanol." Support for new claim 24 can be found throughout the specification as filed. Support for new claim 24 can be found, for example, in the description found in paragraphs [0061] to [0063] of the application as filed. New claim 24 does not introduce any new matter.

New claim 25 has been added which recites "The method of claim 1, wherein the first coating molecule is an oligonucleotide of sequence AGGTCGCCGCCC–thiol and the masking molecule is 6-mercapto-1-hexanol." Support for new claim 25 can be found throughout the specification as filed. Support for new claim 25 can be found, for example, in the description found in paragraphs [0061] to [0065] of the application as filed. New claim 25 does not introduce any new matter.

New claim 26 has been added which recites "The method of claim 1, wherein the first coating molecule is an oligonucleotide of sequence CAGGATGGCGAACAACAAGA–thiol, the second coating molecule is an oligonucleotide of sequence AGGTCGCCGCCC–thiol, and the masking molecule is 6-mercapto-1-hexanol." Support for new claim 26 can be found throughout the specification as filed. Support for new claim 26 can be found, for example, in the description found in paragraphs [0061] to [0065] of the application as filed. New claim 26 does not introduce any new matter.

2. Rejections of the claims

The invention of the pending claims provides electrochemical methods of coating individually-addressable electrodes with the advantageous combination of high purity

and nanoscale resolution. The methods of the present invention enable fabrication integrating large numbers of highly pure coatings of different coating molecules having molecular weight greater than or equal to 800 Da using a novel method employing masking molecules having molecular weight less than or equal to 500 Da. Claim 1 has been amended to clarify and emphasize this important aspect of the present invention, and now recites "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da."

a. Rejection of claims 1-6, 10, 12, and 13 under 35 U.S.C. § 103(a)

The Office Action has rejected claims 1-6, 10, 12, and 13 under 35 U.S.C. § 103(a) as being unpatentable over Tender *et al.* (*Electrochemical Patterning of the Self-Assembled Monolayers onto Microscopic Arrays of Gold Electrodes Fabricated by Laser Ablation*, **Langmuir**, 1996, 12, 5515-5518, herein after referred to as "Tender *et al.*"). In support of these rejections, the Office Action asserts that:

> "Since Tender et al. recognizes that contamination of monolayers may occur on previously coated electrodes and that certain molecules function as a mask for adsorption, it would have been obvious to one having ordinary skill in the art at the time the invention was made to have exposed the electrodes to a masking molecule, because it would minimize the displacement of monolayer constituents by the different alkanethiols in the solution, as suggested by Tender et al."

Applicants respectfully disagree with the characterization of Tender *et al.* in the Office Action, and request reconsideration and withdrawal of the present rejections under 35 U.S.C. § 103(a) in light of the present amendments and the following arguments.

First, Tender *et al.* is not fairly characterized as disclosing or teaching methods of producing electrode arrays employing a reprotection step "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da," as required by the claims as amended with this response. In the context of Tender *et al.*, both EG_6S [molecular weight about 404 Da] and $C_{16}S$

[molecular weight about 416 Da] appear to be referred to as forming a monolayer directly on an electrode. [See, *e.g.*, Tender *et al.*, pg. 5517, first full paragraph]. Applicants submit, therefore, that both $C_{16}S$ and EG_6S appear to be acting as **coating** molecules on different electrodes in Tender *et al.*, and that Tender *et al.* is more properly characterized as teaching the **coating** of bare electrodes with molecules of molecular weight of about 404 Da and 416 Da. Tender *et al.* is therefore fairly characterized as **not** teaching a method of producing electrode arrays employing a reprotection step, let alone a reprotection step "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." as provided by the claims as amended with this response. The difference in molecular weight between masking molecules and coating molecules appears to be an aspect of technical significance important to the production of highly pure electrode arrays using the method of the claimed invention. For example, the importance of the difference in molecular weights between the coating and masking molecules is highlighted, *e.g.*, in paragraphs [0035] of the application as filed:

> [**0035**] Generally the masking molecule will have relatively low molecular weight, for instance **below 500**, in particular **below 200 or 150**. Smaller masking molecules are preferred **as these are more effective at reprotection in the reprotection step (e)** discussed further below. **They also form a dense monolayer, which is advantageous**. (Emphasis added).

Applicants assert, therefore, that it would not have been obvious to one of ordinary skill in the art at the time of the invention to include a reprotection step "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da," because Tender *et al.* does not suggest, or even contemplate, methods employing masking and coating molecules having these specific molecular weight characteristics.

Second, the scope of the cited prior art is deficient with respect to key aspects of the present invention as claimed and Applicants assert that this deficiency of the cited art extends well beyond a reasonably predictable variation of the individually addressable array fabrication techniques described in Tender *et al.* [*See*, Examination Guidelines for Determining Obviousness Under 35 U.S.C 103 in View of the Supreme Court decision in KSR International Co. V. Teleflex Inc., Fed. Register, Vol. 72. No. 195 (2007): "When considering obviousness of a combination of known elements, the operative question is whether the improvement is more than the predictable use of prior art elements according to their established functions"]. The invention of the rejected claims is not merely routine optimization of known methods of producing individually addressable arrays. Rather, the invention as claimed relates to a fundamentally distinct electrode fabrication approach that significantly reduces electrode contamination using a reprotection step "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da," in contrast to the approach of Tender *et al.* of using low concentrations of alkanethiols, short immersion times, and/or analogous disulfides.

Tender *et al.* does not, therefore, render obvious claims 1-6, 10, 12, and 13 because it fails to disclose, teach or suggest all the limitations of the rejected claims as amended herein. The missing limitations, furthermore, were well outside the grasp of the skilled artisan at the time of the invention. Accordingly, Applicants request reconsideration and withdrawal of the present rejections under 35 U.S.C § 103(a).

b. Rejection of claims 7-9 under 35 U.S.C. § 103(a)

The Office Action has rejected claims 7-9 under 35 U.S.C. § 103(a) as being unpatentable over Tender *et al.* in view of International Patent Application Publication No. WO/1999/51778 (herein after referred to as "Barton *et al.*"). In support of these rejections, the Office Action asserts that:

> "It would have been obvious to one having ordinary skill in the art at the time the invention was made to have deposited the oligonucleotides of Barton et al. in the method of Tender et al., because it would enable the electrodes to function as a biosensor for the detection of genetic mutations in the nucleic acid sequences."

Applicants respectfully disagree with the characterization of Tender *et al.* and Barton *et al.* in the Office Action, and request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) in light of the present amendments and following arguments.

Applicants reiterate their arguments with respect to the rejection of claims 1-6, 10, 12, and 13 based upon Tender *et al.* Specifically, Applicants assert that Tender *et al.* does not teach or suggest an electrode fabrication method "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." Likewise, the disclosure in Barton *et al.* is limited to detection of genetic point mutations in nucleic acid sequences employing a preexisting electrode or multi-electrode array and does not provide for methods of producing an individually addressable electrode array. Therefore, it would not have been obvious to one of ordinary skill in the art at the time of the invention to combine Tender *et al.* and Barton *et al.* to arrive at the reprotection multi-electrode array production method of the present invention "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." Accordingly, reconsideration and withdrawal of the rejection of claims 7-9 is respectfully requested.

c. Rejection of claim 11 under 35 U.S.C. § 103(a)

The Office Action has rejected claim 11 under 35 U.S.C. § 103(a) as being unpatentable over Tender *et al.* in view of U.S. Pat. No. 6,355,420 (herein after referred to as "Chan"). In support of this rejection, the Office Action asserts that:

> "It would have been obvious to one having ordinary skill in the art at the time the invention was made to have applied an electric field, as taught by Chan, in the method of Tender et al., because it would align the coating

> molecules, such as DNA molecules or other polymers, in the direction of the electric field (column 85 lines 19-23 of Chan). The application of the electric field is either AC or DC, since an electrical potential for providing the electric field can only be applied by either AC or DC."

Applicants respectfully disagree with the characterization of Tender *et al.* and Chan in the Office Action, and request reconsideration and withdrawal of the present rejections under 35 U.S.C. § 103(a) in light of the present amendments and following arguments.

Applicants reiterate their arguments with respect to the rejection of claims 1-6, 10, 12, and 13 based upon Tender *et al.* Specifically, Applicants assert that Tender *et al.* does not teach or suggest an electrode fabrication method "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." Likewise, the disclosure in Chan is limited to the orientation of polymers in an electric field and does not provide for methods of producing an individually addressable electrode array. Therefore, it would not have been obvious to one of ordinary skill in the art at the time of the invention to combine Tender *et al.* and Chan to arrive at the reprotection multi-electrode array production method of the present invention "wherein the first coating molecule and the second coating molecule each have a molecular weight greater than or equal to 800 Da; and wherein the masking molecule has a molecular weight less than or equal to 500 Da." Accordingly, reconsideration and withdrawal of the rejection of claim 11 is respectfully requested.

CONCLUSION

In view of the foregoing arguments, this case is considered to be in condition for allowance and passage to issuance is respectfully requested. If new issues of patentability are raised, the Examiner is invited to call and arrange for an opportunity to discuss these issues via telephone interview.

It is believed that a 2-month extension of time and corresponding fee of $490.00 is required for this submission, pursuant to 37 C.F.R. §1.17(a). Also, it is believed that $312 is due for the addition of 6 claims in excess of 20, pursuant to 37 C.F.R. §1.16(i).

Therefore, payment in the total amount of $802.00 is being made via the Electronic Filing System with this submission. If this is incorrect or if any additional fees or further extensions of time are required, however, please deduct the appropriate fees required for this submission and any extension of time required from Deposit Account No. 07-1969.

Respectfully submitted,

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